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Association of Sleep Characteristics and Cognition in Older Community-Dwelling Men: the MrOS Sleep Study

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Study Objectives: To examine the association of objectively and subjectively measured sleep characteristics with cognition in older men.
Design: A population-based cross-sectional study.
Setting: 6 centers in the United States.
Participants: 3,132 community-dwelling older men (mean age 76.4 ± 5.6 years).
Interventions: None.
Measurements and Results: Objectively measured sleep predictors from wrist actigraphy were total sleep time (TST), sleep efficiency (SE), and wake after sleep onset (WASO). Subjective sleep predictors were self-reported poor sleep (Pittsburgh Sleep Quality Index [PSQI] > 5), excessive daytime sleepiness (EDS, Epworth Sleepiness Scale Score > 10), and TST. Cognitive outcomes were measured with the Modified Mini-Mental State examination (3MS), the Trails B test, and the Digit Vigilance Test (DVT). After adjustment for multiple potential confounders, WASO was modestly related to poorer cognition. Compared to those with WASO < 90 min, men with WASO ≥ 90 min took 6.1 sec longer to complete the Trails B test and had a 0.9-point worse 3MS score, on average (P < 0.05). Actigraphically measured long sleepers had a slightly worse 3MS score compared to those with 7-8 h of sleep, but had similar Trails B and DVT completion times. Compared to those who self-reported sleeping 7-8 h, long sleepers (> 8 h) on average took 8.6 sec more to complete the Trails B test, had a 0.6-point worse 3MS score, and took 46 sec longer to complete the DVT (P < 0.05). PSQI and EDS were not independently related to cognitive outcomes.
Conclusions: There were modest cross-sectional associations of WASO and self-reported long sleep with cognition among older community-dwelling men. EDS and PSQI were not related to cognition.
Keywords: Sleep fragmentation, total sleep time, cognitive function, aging
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INTRODUCTION

At least 10% of people 65 years old or older will develop cognitive impairment, with the rate rising exponentially with advancing age.[1,2] With life expectancies rising this number will grow in future years, increasing the importance of identifying factors related to cognitive impairment among older adults which may lead to preventative strategies. As many as 50% of older adults report habitual sleep problems, including chronic insomnia.[3-5] The association between both subjectively and objectively measured sleep characteristics and cognitive function has received little attention.

Past studies of the relation of sleep characteristics to cognition have predominantly focused on self-reported total sleep time (TST) and sleep quality,[6-12] with most finding an association between both self-reported long sleep duration and self-reported sleep complaints and lower levels of cognitive function. A few studies examined the association of objectively measured TST and sleep fragmentation with cognitive function and found little association between TST and cognition and conflicting results regarding sleep fragmentation.[13-18] Of note, most previous studies of the association of sleep characteristics and cognitive function have been done in specific populations with clinical disorders, such as patients with insomnia or sleep disordered breathing.[15,17,19,20] Few large studies of community-dwelling older adults have focused on objective measures of sleep.[13,16,18]

While these past studies have added to the understanding of the relationship between sleep and cognition, none have addressed the association of both subjectively and objectively measured sleep parameters and cognition in a large cohort of community-dwelling men. In particular, no study has examined both self-report and objectively measured TST in relation to cognition. This analysis examined the cross-sectional relationship of subjective and objective sleep parameters and cognitive function with data gathered in the Outcomes of Sleep Disorders in Older Men (MrOS Sleep) Study.

METHODS

Participants

During the Osteoporotic Fractures in Men Study (MrOS) baseline examination from 2000 to 2002, 5,994 community-

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dwelling men 65 years or older were enrolled at 6 clinical centers in the United States: Birmingham, Alabama; Minneapolis, Minnesota; Palo Alto, California; the Monongahela Valley near Pittsburgh, Pennsylvania; Portland, Oregon; and San Diego, California.[21,22] In order to participate, men needed to be able to walk without assistance and must not have had a bilateral hip replacement.

The MrOS Sleep Study, an ancillary study of the parent MrOS cohort, was conducted between December 2003 and March 2005 and recruited 3,135 of these participants (exceeding the goal of 3,000 participants) for a comprehensive sleep assessment. Men were screened for nightly use of mechanical devices during sleep, including pressure mask for sleep apnea (CPAP or BiPAP), mouthpiece for snoring or sleep apnea, or oxygen therapy and were generally excluded; however, the study sample includes 49 men who reported use of one of these devices. Of the 2,859 MrOS men who did not participate in this ancillary study, 344 died before the sleep visit, 36 had already terminated the study, 332 were not asked because recruitment goals had already been met, 150 were not eligible, and 1,997 refused. Cognitive function data was available for 3,132 men. All of these men had data on subjective sleep measures, and 3,053 underwent wrist actigraphy.

All men provided written informed consent, and the study was approved by the institutional review board at each site.

Sleep Parameters

Objective actigraphic parameters of sleep-wake patterns

Objective characteristics of sleep-wake patterns were estimated using an actigraph (SleepWatch-O, Ambulatory Monitoring, Inc., Ardsley, NY) worn continuously for a minimum of 5 nights (mean ± SD, 5.2 ± 0.9 nights). Participants were instructed to wear the actigraph securely fastened around their non-dominant wrist, to be removed only when bathing or during water sports. The actigraph is similar in size and weight to a standard wristwatch, and movement is detected via a piezoelectric bimorph-ceramic cantilever beam that generates a voltage each time the actigraph is moved. These voltages are gathered continuously and summarized over 1-min intervals. Actigraphy has been shown to provide a reliable estimate of sleep-wake patterns.[23] Data were collected in 3 modes but are reported here based on digital integration mode (also known as proportional integration mode).[24] ActionW-2 software (Ambulatory Monitoring, Inc., Ardsley, NY) was used to analyze the actigraphy data.[25] Details of the actigraphy scoring algorithms utilized in the study have been published elsewhere.[26,27]

Participants completed sleep diaries for the time period they wore the actigraph. The diaries included time into and time out of bed and times the actigraph was removed. This information was used in editing the actigraphy data files to set intervals for when the participant was in bed trying to sleep (after "lights off"), and to delete time when the actigraph was removed. Interscorer reliability for editing the actigraphy data files has been previously found to be high in our group (intra-class coefficient = 0.95), and actigraphy has been shown to have good concordance with TST from polysomnography.[26,28]

Variables estimated from actigraphy used in this analysis included: (1) total sleep time (TST): h per night spent sleeping while in bed after "lights off"; (2) sleep efficiency (SE): percentage of time in bed after "lights off" spent sleeping; (3) wake after sleep onset (WASO): minutes of wake after sleep onset during the in bed interval, with sleep onset defined as the point when the participant achieved a 20-min continuous block of sleep after "lights off"; (4) number of long wake episodes (LWEP): number of awakenings ≥ 5 min in duration while in bed. All exposure variables from actigraphy reflect data averaged over all nights they wore the device in order to obtain a more representative characterization of usual sleep patterns.

Self-reported sleep parameters

Participants completed the Pittsburgh Sleep Quality Index (PSQI), a validated measure of subjective sleep quality and sleep disturbances over a one-month time period. Global PSQI scores range from 0-21, and a score > 5 is indicative of poor sleep.[29] The Epworth Sleepiness Scale (ESS), a self-administered questionnaire, was used to classify subjective daytime sleepiness. Scores on the ESS range from 0-24, with a score > 10 indicating excessive daytime sleepiness (EDS).[30,31] In addition, participants were asked about TST with the question "On most nights, how many hours do you sleep each night?", with data collected rounded to the hour.

Cognitive Function

Three cognitive function tests were administered by trained clinic staff: the Modified Mini-Mental State examination (3MS), the Trail Making Test-Part B (Trails B), and the Digit Vigilance Test (DVT).

The 3MS is a global measurement of cognitive function, with components for orientation, concentration, language, praxis, and immediate and delayed memory. Scores on the 3MS range from 0 to 100, with higher scores representing better cognitive functioning.[32]

The Trails B is a timed test that measures attention, sequencing, visual scanning, and executive function. The participant continuously scans a page to identify numbers and letters in a specified sequence while shifting from number to letter sets.[33,34] A faster time for completion (in seconds) represents better cognitive functioning.

The DVT is a paper-and-pencil test designed to measure vigilance during rapid visual tracking and accurate selection of target stimuli.[35] The standard test requires participants cross out 6s which appear randomly within 59 rows of 35 single digits. This test was modified to increase difficulty by requiring participants to cross out only those 6s that are followed by a number higher than 6 (7, 8, or 9). A faster time for completion (in seconds) represents better cognitive functioning.

Other Measurements

All participants completed questionnaires, which included items about demographics, medical history, self-reported health status, physical activity, smoking, caffeine intake, and alcohol use. The number of prior medical conditions was calculated as the summed total of prior diagnoses of common chronic illnesses (stroke or transient ischemic attack, diabetes, Parkinson disease, chronic obstructive pulmonary disease (COPD), hypertension, coronary heart disease). Participants were asked to bring in all current medications used within the preceding 30

days. All prescription and nonprescription medications were entered into an electronic database and each medication was matched to its ingredient(s) based on the Iowa Drug Information Service (IDIS) Drug Vocabulary (College of Pharmacy, University of Iowa, Iowa City, IA).[36] The use of antidepressants, benzodiazepines, and sleep medications (non-benzodiazepine, non-barbiturate sedative hypnotics) were categorized. The Geriatric Depression Scale (GDS) was used to assess depressive symptoms, with higher scores corresponding to higher levels of depression.[37,38] Level of physical activity was assessed using the physical activity scale for the elderly (PASE).[39] Functional status was assessed by collecting information on 5 instrumental activities of daily living (IADL), which included walking 2 to 3 blocks on level ground, climbing up to 10 steps, preparing meals, doing heavy housework, and shopping for groceries or clothing.[40,41] Self-reported caffeine intake was calculated based on answers to questions regarding intake of caffeinated coffee, tea, and soda.[42]

A comprehensive examination included measurements of body weight and height. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters.

Statistical Analysis

For the primary analyses, the predictor variables were expressed as categorical variables which were defined similarly to previous publications for comparability (TST ≤ 5 h, > 5 to 7 h, > 7 to 8 h, > 8 h; SE < 70% vs. ≥ 70%; WASO ≥ 90 min vs. < 90 min; number of long wake episodes ≥ 8 vs. < 8) or used standard cutpoints (PSQI > 5 vs. ≤ 5; ESS > 10 vs. ≥ 10). Analyses were also performed to evaluate the linear relationship of the sleep parameters and cognition, with the sleep parameters expressed as continuous variables.

Characteristics of participants were compared across categories of objectively measured TST using χ^2 tests for categorical variables, analysis of variance (ANOVA) for normally distributed continuous variables, and Kruskal-Wallis tests for continuous variables with skewed distributions. Similar comparisons were performed across categories of the other sleep predictors (data not shown).

The association between a given sleep characteristic and cognitive function outcome was examined with linear regression models. The cognitive scores were transformed to meet model requirements (cube transformation for 3MS, log transformation for both Trails B and DVT) and back-transformed for display of results. All models were adjusted for multiple confounders. Covariates were included in the multivariable models if they were related to one or more of the cognitive outcomes and one or more of the sleep parameters at $P < 0.10$. Results are presented as adjusted means and 95% confidence intervals for the categorical representation of the predictors, β coefficients and p-values for the continuous representation of the predictors. The β coefficients are presented as a 1 SD decrease for SE, a 30-min decrease for WASO, a 1-h decrease for TST, and a 1 SD increase for the PSQI and ESS. The R^2 for the models are presented to show the amount of variation of the outcome that was explained by all variables in the model combined, along with the partial r^2 for the specific sleep predictor to show the amount of variation that was explained by the sleep predictor in addition to all other covariates in the model.

In secondary analyses, models with the predictor of TST were further adjusted by WASO to determine if associations were driven by underlying sleep fragmentation. Models with the predictor of sleep fragmentation were further adjusted by ESS to determine if associations were driven by daytime sleepiness. To enable comparability to other studies with much older populations, the interactions of the sleep parameters with age (< 80 vs ≥ 80 years old) were explored. Stratifications by age category was performed where appropriate (when interaction $P < 0.10$). Analyses were performed examining the association of the sleep predictors significantly related to the 3MS score with the subscores of the 3MS to determine if a specific component was driving the association. Lastly, although all analyses were prespecified, a Bonferroni correction was applied to all significant P-values in the primary analysis to examine if the associations observed held after correction for multiple comparisons.

All significance levels reported were 2-sided and all analyses were conducted using SAS version 9.2 (SAS Institute Inc, Cary, NC).

RESULTS

Characteristics of the Study Population

The analysis cohort comprised 3,132 men with data for cognitive outcomes and data for one or more sleep predictors. Of the 3,053 men with actigraphy data, 251 (8.2%) had < 5 nights of data collected: 181 had 4 nights of data, 49 had 3 nights of data, 10 had 2 nights of data, and 11 had 1 night of data. The men had an average age of 76 ± 6 years, and 90% were Caucasian. Almost half of the men (44%) had self-reported poor sleep quality defined as PSQI > 5, and 13% had self-reported excessive daytime sleepiness (ESS > 10, Table 1). The overall average of both self-reported and objectively measured TST was similar (self-reported 6.9 ± 1.2 h; objectively measured 6.4 ± 1.2 h), with approximately 12% of men with ≤ 5 h of sleep per night (self-reported 11.7%, objective 12.3%) and about 6% had a long sleep duration (> 8 h per night ; self-reported 5.5%, objective 7.2%). Though rates of long and short sleep duration were similar for the self-reported and objectively measured TST, there was only 50% agreement between the 2 measures across the categories, and the correlation of the linear representations was modest (r = 0.31). Among categories of TST, those with self-reported long and short sleep duration had the highest levels of WASO on average (TST ≤ 5: 85.4 min; TST > 5 to 7: 75.6; TST > 7 to 8: 78.4 min; TST > 8: 93.0 min; $P < 0.001$) while the amount of WASO decreased linearly across categories of objectively measured TST (TST ≤ 5: 128.6 min; TST > 5 to 7: 78.4; TST > 7 to 8: 58.8 min; TST > 8: 58.7 min; $P < 0.001$). Men had an average SE of 78%, an average WASO of 78 min, and an average of 7 long wake episodes. The mean of the cognitive function outcomes for the cohort were as follows: 92.6 ± 6.4 points for the 3MS, 122.2 ± 55.3 sec for Trails B, and 558.4 ± 191.7 sec for the DVT.

Many covariates differed significantly across categories of objectively measured TST (Table 2). Those with long sleep duration (> 8 h) on average were older, had higher rates of antidepressant use, were less physically active, and had better self-reported health ($P < 0.03$). Those with short sleep duration (≤ 5 h) were on average heavier, more likely to be a minority, had a higher num-

Table 1—Summary of sleep predictors and cognitive outcomes

Characteristic	All Participants (N = 3132)
Objective sleep	
Sleep efficiency, %	78.1 ± 12.0
Sleep efficiency < 70%	582 (19.1)
WASO, min	78.4 ± 44.3
WASO ≥ 90 min	977 (32.0)
# of long wake episodes	6.9 ± 3.3
≥ 8 long wake episodes	1006 (33.0)
Actigraphic TST, h	6.4 ± 1.2
≤ 5 h	376 (12.3)
> 5 to 7 h	1712 (56.1)
> 7 to 8 h	745 (24.4)
> 8 h	220 (7.2)
Subjective sleep	
Self-reported TST, h	6.9 ± 1.2
≤ 5 h	365 (11.7)
> 5 to 7 h	1780 (56.9)
> 7 to 8 h	813 (26.0)
> 8 hrs	173 (5.5)
PSQI (range 0-21)	5.6 ± 3.3
PSQI > 5	1383 (44.2)
ESS (range 0-24)	6.2 ± 3.7
ESS > 10	405 (12.9)
Cognitive outcomes	
3MS score (range 0-100)	92.6 ± 6.4
Trails B completion time, sec	122.2 ± 55.3
DVT completion time, sec	558.4 ± 191.7

Data shown as mean ± SD or n (%). WASO, wake after sleep onset; TST, total sleep time; PSQI, Pittsburgh Sleep Quality Index; ESS, Epworth Sleepiness Scale; 3MS, Modified Mini-Mental State examination; DVT, Digit Vigilance Test.

ber of medical conditions including diabetes and COPD, were less educated, and were more likely to smoke ($P < 0.05$). There was a slight U-shaped pattern for some covariates: There were higher rates of IADL impairment, hypertension, stroke, and depression in both the long and short sleepers ($P < 0.05$).

Associations between Objectively Measured Sleep Parameters and Cognition

Objectively measured long sleep duration was associated with the 3MS score, with long sleepers having about a 1-point decrease in 3MS score, on average, compared to those sleeping > 7 to 8 h per night after multivariate adjustment for age, race, clinic, education, depression, BMI, number of IADLs, comorbidities, antidepressant use, benzodiazepine use, alcohol use, smoking, physical activity, and self-reported health status (Table 3). This association was not seen for Trails B and DVT (Tables 4 and 5). The multivariate model including TST explained about 21% of the overall variance in 3MS score, with long sleep explaining 0.4%. The association of long sleep duration and the 3MS persisted after further adjustment for WASO. Long sleep duration was associated to the 3MS subscore for delayed recall, but no other subscores. Short sleep duration showed no associations to cognitive function in this cohort (Tables 3-5).

After adjustment for multiple confounders, a number of measures of increased sleep fragmentation were associated with worse levels of cognitive function. WASO was associated to the Trails B test (men with WASO ≥ 90 min took 6.1 sec longer to complete on average) and the 3MS score (men with WASO ≥ 90 min had an 0.6 worse average score). The number of long wake episodes was associated to the 3MS score (men with ≥ 8 episodes had 0.6 worse average score). Multivariate models explained about 21% of the overall variance in the 3MS score, with WASO ≥ 90 min explaining about 0.8%, and 20% of the overall variance for Trails B with WASO ≥ 90 min explaining 1.2%. For comparison, the partial r^2 for age in these models was about 7% for the 3MS outcome and 10% for the Trials B outcome (Tables 3 and 4). These associations of sleep fragmentation with cognition persisted after further adjustment for sleepiness (ESS). Sleep fragmentation measures were associated with two 3MS subscores related to memory (delayed recall and temporal orientation) and naming.

When objectively measured sleep parameters were modeled continuously their associations with cognition were largely similar, but there was greater evidence supporting independent associations and larger percentages of variation explained by the continuous predictors. When examined as a continuous predictor, the associations of SE and the number of long wake episodes with the Trails B was also significant. There was a 2.24 longer Trails B test time, on average, for each decrease of 1 SD (12%) in SE and a 0.81-sec average longer test completion time per 1 episode increase in the number of long wake episodes. The association of WASO and DVT was also significant, with a 4.8-sec average longer test completion time per 30-min increase in WASO (Tables 3-5).

Associations between Self-Reported Sleep Parameters and Cognition

After adjustment, there were no significant associations between PSQI or excessive daytime sleepiness (ESS > 10) and cognition (Tables 3-5). There was an apparent U-shaped association of self-reported sleep time with cognition as assessed by the 3MS (Tables 3). Those men with short (≤ 5 h) and long (> 8 h) sleep duration had lower levels of cognition, on average, compared to those with > 7 to 8 h of self-reported sleep per night. Self-reported sleep was related to the 3MS subscores for spatial orientation, writing, and immediate recall. Long but not short self-reported sleep duration was related to longer Trails B and DVT test completion times after multivariate adjustment. Long sleepers took an average of 8.4 sec longer to complete the Trails B test and 46.2 sec longer for the DVT than those who reported sleeping > 7 to 8 h per night. Further adjustment by WASO attenuated these results. There was no longer an association with long sleep duration and Trails B, and the association of long sleep duration with the 3MS was no longer statistically significant ($P = 0.056$).

Linear associations with the subjective sleep parameters and cognition were largely similar. After multivariate adjustment there was no linear association with self-reported sleep and cognition.

Table 2—Baseline characteristics by objectively measured TST

Characteristic	≤ 5 h (N = 376)	> 5 to 7 h (N = 1712)	> 7 to 8 h (N = 745)	8+ h (N = 220)	P-value
Age, y	76.5 ± 5.7	76.1 ± 5.4	76.5 ± 5.7	77.8 ± 5.9	< 0.01
BMI, kg/m^2	29.3 ± 4.8	27.1 ± 3.7	26.5 ± 3.5	26.8 ± 3.5	< 0.01
Race/Ethnicity					
Caucasian	326 (86.7)	1537 (89.8)	682 (91.5)	202 (91.8)	< 0.01
African American	28 (7.5)	62 (3.6)	19 (2.6)	6 (2.7)	
Other	22 (5.9)	113 (6.6)	44 (5.9)	12 (5.5)	
Any IADLs	112 (29.8)	347 (20.3)	141 (18.9)	50 (22.7)	< 0.01
Medical conditions					
Hypertension	214 (56.9)	837 (48.9)	359 (48.2)	113 (51.4)	0.03
Stroke or TIA	55 (14.6)	157 (9.2)	90 (12.1)	31 (14.1)	< 0.01
Diabetes	68 (18.1)	219 (12.8)	93 (12.5)	29 (13.2)	0.04
Parkinson disease	6 (1.6)	16 (0.9)	11 (1.5)	5 (2.3)	0.27
COPD	29 (7.7)	94 (5.5)	27 (3.6)	10 (4.6)	0.03
CHD*	145 (38.7)	541 (31.7)	235 (31.5)	70 (31.8)	0.06
# of medical conditions**					
None	182 (48.4)	1029 (60.1)	444 (59.6)	134 (60.9)	< 0.01
1-2	106 (28.2)	439 (25.7)	189 (25.4)	55 (25.0)	
3+	88 (23.4)	243 (14.2)	112 (15.0)	31 (14.1)	
Antidepressant use	35 (9.3)	122 (7.1)	52 (7.0)	31 (14.2)	< 0.01
Benzodiazepine use	19 (5.1)	67 (3.9)	37 (5.0)	15 (6.9)	0.19
Sleep medication use	9 (2.4)	36 (2.1)	15 (2.0)	2 (0.9)	0.64
GDS score	2.2 ± 2.2	1.7 ± 2.1	1.8 ± 2.3	1.9 ± 2.2	< 0.01
Education					
< High school	28 (7.5)	93 (5.4)	26 (3.5)	15 (6.8)	< 0.01
High school	76 (20.2)	273 (16.0)	104 (14.0)	35 (15.9)	
> High school	272 (72.3)	1346 (78.6)	615 (82.6)	170 (77.3)	
Alcohol use, drinks/week					
0-2	226 (60.6)	1030 (60.4)	415 (55.9)	129 (59.5)	0.06
3-13	124 (33.2)	592 (34.7)	283 (38.1)	68 (31.3)	
14+	23 (6.2)	83 (4.9)	45 (6.1)	20 (9.2)	
Smoking					
Never	124 (33.0)	688 (40.2)	299 (40.1)	93 (42.3)	< 0.01
Past	234 (62.2)	994 (58.1)	433 (58.1)	125 (56.8)	
Current	18 (4.8)	30 (1.8)	13 (1.7)	2 (0.9)	
Caffeine use, mg/day	261 ± 266	237 ± 249	229 ± 241	200 ± 196	0.13
PASE physical activity score	140.0 ± 75.0	150.2 ± 72.3	140.6 ± 69.3	138.3 ± 69.6	< 0.01
Self-rated health good/excellent	311 (82.7)	1499 (87.6)	636 (85.4)	197 (89.6)	0.03

Data shown as mean ± SD or n (%). P-values for continuous data are from an ANOVA for normally distributed data, Kruskal-Wallis test for skewed data. P-values for categorical data are from a χ^2 test for homogeneity. *Coronary heart disease includes myocardial infarction, angina, congestive heart failure, bypass surgery, angioplasty, or heart valve replacement. **Medical conditions include stoke/TIA, coronary heart disease, diabetes mellitus, COPD, Parkinson disease, and hypertension. TST, total sleep time; BMI, body mass index; IADL, instrumental activities of daily living; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; GDS, geriatric depression scale; PASE, physical activity scale for the elderly.

Interactions with Age

There was a significant interaction of age with WASO and the number of long wake episodes for the continuous outcome of the DVT completion time ($P \leq 0.04$, Figure 1). Those aged ≥ 80 years showed a larger association with the sleep fragmentation measures and DVT than those < 80. Among those ≥ 80, there was an average 9.26-sec longer time to complete the DVT per 1 SD decrease in SE ($P = 0.01$).

Bonferroni Correction

In Tables 3-5 we performed 14 models per outcome, a total of 42 models. Adjusting the significance level of 0.05 with a Bonferroni correction would lead to a significance cutpoint of $P < 0.0011$ (= 0.05/42). After applying this more stringent cutpoint for significance to the these results a number of significant associations persisted: WASO used as a continuous predictor with both the 3MS and Trails B, the categorical representation

Table 3—Sleep characteristics and 3MS score

Sleep Characteristic	Adjusted Means (95% CI) or β Coefficient (P-value)	R^2 for Model	Partial r^2 for the predictor	% of R^2 Explained by this predictor
Objective actigraphic parameters				
Sleep efficiency				
< 70%	93.1 (92.7, 93.5)	0.2105	0.0021	1.00
≥ 70% (ref)	93.1 (92.9, 93.3)	–	–	–
Continuous, per 1 SD decrease	-0.19 (0.06)	0.2115	0.0071	3.35
Wake after sleep onset				
< 90 min (ref)	93.3 (93.1, 93.5)	–	–	–
≥ 90 min	**92.7 (92.4, 93.0)**	0.2130	0.0085	3.98
Continuous, per 30-min increase	**-0.29 (< 0.01)**	0.2153	0.0184	8.56
Number of long wake episodes				
< 8 (ref)	93.3 (93.1, 93.5)	–	–	–
≥ 8	**92.7 (92.4, 93.0)**	0.2126	0.0070	3.29
Continuous, per 1 episode increase	**-0.11 (< 0.01)**	0.2139	0.0136	6.35
Actigraphic total sleep time				
≤ 5 h	93.2 (92.7, 93.7)	0.2137	0.0004	0.18
> 5 to 7 h	93.3 (93.0, 93.5)	0.2137	0.0028	1.32
> 7 to 8 h (ref)	93.0 (92.6, 93.3)	–	–	–
> 8 h	**92.1 (91.4, 92.7)**	0.2137	0.0042	1.96
Continuous, per 1-h decrease	**0.20 (0.01)**	0.2122	0.0009	0.42
Subjective sleep				
Self-reported total sleep time				
≤ 5 h	**92.4 (91.9, 92.9)**	0.2200	0.0094	4.27
> 5 to 7 h	93.2 (93.0, 93.4)	0.2200	0.0009	0.43
> 7 to 8 h (ref)	93.2 (92.8, 93.5)	–	–	–
> 8 h	**92.3 (91.5, 93.0)**	0.2200	0.0058	2.66
Continuous, per 1-h decrease	-0.06 (0.41)	0.2169	0.0020	0.93
Pittsburgh Sleep Quality Index				
≤ 5 (ref)	93.1 (92.9, 93.3)	–	–	–
> 5	93.0 (92.7, 93.3)	0.2169	0.0061	2.81
Continuous, per 1 SD increase	-0.06 (0.55)	0.2169	0.0110	5.09
Epworth Sleepiness Scale				
≤ 10 (ref)	93.1 (92.9, 93.2)	–	–	–
> 10	93.0 (92.6, 93.5)	0.2168	0.0018	0.85
Continuous, per 1 SD increase	**0.22 (0.01)**	0.2183	0.0001	0.05

Bold = P < 0.05. All results adjusted for age, race, clinic, BMI, instrumental activities of daily living, comorbidities, antidepressant use, benzodiazepine use, Geriatric Depression Scale score, education, alcohol use, smoking, physical activity, and self-reported health status.

of WASO and Trails B, the continuous representation of the number of long wake episodes and the 3MS, and self-reported long sleep duration and the DVT.

DISCUSSION

This cross-sectional analysis of 3,132 older community-dwelling men suggests a modest association of cognition with objectively measured sleep fragmentation (WASO, SE) and self-reported long sleep duration. These men had high levels of cognitive functioning. While they had a high rate of self-reported poor sleep quality, the average TST was between 6 and 7 h per night and the average SE was 78%.

Impaired sleep continuity may cause sleepiness, which although not detectable by subjective reports, may result in reduced vigilance. This reduced vigilance may negatively influence executive functioning.[20,43,44] Such effects may be anticipated to be magnified in settings of increased vulnerability.[45] The results of our secondary analyses are consistent with this, demonstrating larger sleep related cognitive deficits in the very elderly members of our cohort. While sleep fragmentation may be related to sleepiness, sleepiness did not completely mediate the association of sleep fragmentation with cognition. In this cohort, the associations persisted after further adjustment for daytime sleepiness; however, we did not formally test for mediation in these models.

Of the associations between sleep fragmentation and cognition, the most consistent relationship was seen between cognition and WASO, which explained more of the overall variability in the cognitive outcome measures. The somewhat less consistent findings observed for SE may relate to greater measure-

Table 4—Sleep characteristics and Trail Making B test completion time (sec)

Sleep Characteristic	Adjusted Means (95% CI) or β Coefficient (P-value)	R^2 for Model	Partial r^2 for the predictor	% of R^2 Explained by this predictor
Objective actigraphic parameters				
Sleep efficiency				
< 70%	114.4 (110.8, 118.1)	–	–	–
≥ 70% (ref)	110.8 (109.2, 112.5)	0.1972	0.0065	3.28
Continuous, per 1 SD decrease	**2.24 (0.03)**	0.1978	0.0097	4.92
Wake after sleep onset				
< 90 min (ref)	109.6 (107.8, 111.4)	–	–	–
≥ 90 min	**115.7 (112.9, 118.5)**	0.2000	0.0122	6.12
Continuous, per 30-min increase	**3.26 (< 0.01)**	0.2026	0.0235	11.62
Number of long wake episodes				
< 8 (ref)	110.5 (108.7, 112.3)	–	–	–
≥ 8	113.6 (110.9, 116.3)	0.1973	0.0063	3.20
Continuous, per 1 episode increase	**0.81 (< 0.01)**	0.1983	0.0122	6.14
Actigraphic total sleep time				
≤ 5 h	111.8 (107.5, 116.3)	0.1994	0.0011	0.57
> 5 to 7 h	**109.7 (107.8, 111.7)**	0.1994	0.0039	1.96
> 7 to 8 h (ref)	113.4 (110.4, 116.5)	–	–	–
> 8 h	118.9 (113.0, 125.0)	0.1994	0.0026	1.30
Continuous, per 1-h decrease	-1.53 (0.06)	0.1974	0.0003	0.16
Subjective sleep				
Self-reported total sleep time				
≤ 5 h	115.9 (111.4, 120.6)	0.1993	0.0062	3.12
> 5 to 7 h	110.7 (108.8, 112.6)	0.1993	0.0008	0.42
> 7 to 8 h (ref)	111.0 (108.2, 114.0)	–	–	–
> 8 h	**119.4 (112.7, 126.5)**	0.1993	0.0060	2.99
Continuous, per 1-h decrease	0.59 (0.49)	0.1969	0.0014	0.71
Pittsburgh Sleep Quality Index				
≤ 5 (ref)	111.8 (109.8, 113.9)	–	–	–
> 5	111.8 (109.5, 114.1)	0.1968	0.0053	2.68
Continuous, per 1 SD increase	0.84 (0.34)	0.1970	0.0134	6.80
Epworth Sleepiness Scale				
≤ 10 (ref)	112.1 (110.5, 113.7)	–	–	–
> 10	109.9 (105.9, 114.2)	0.1970	0.0001	0.06
Continuous, per 1 SD increase	**-1.94 (0.02)**	0.1983	< 0.0001	0.01

Bold = P < 0.05. All results adjusted for age, race, clinic, BMI, instrumental activities of daily living, comorbidities, antidepressant use, benzodiazepine use, Geriatric Depression Scale score, education, alcohol use, smoking, physical activity, and self-reported health status.

ment error due to inaccuracies in identifying "lights off" time. Our findings are consistent with those of other research that have similarly found modest associations with objectively measured sleep fragmentation and cognition.[15,16] Similar analyses were performed in the Study of Osteoporotic Fractures (SOF) on a much older population of community-dwelling women (average age 83.5 years).[13] The associations with sleep fragmentation and cognition were larger in magnitude in the SOF study than those found in this younger MrOS cohort. Consistent with that finding, in the current analysis there was a significant interaction between age and sleep fragmentation for the DVT test, with stronger associations seen in those men 80 years old or older.

The association of cognition with TST measured both subjectively and objectively was examined. A U-shaped relationship with self-reported TST and the 3MS score was observed, with those with short and long sleep duration scoring worse on average. The association of objectively measured TST and the 3MS score was not U-shaped, but showed lower scores on the 3MS for the long sleepers. This association with long sleep duration and lower cognitive function was also seen with self-reported TST and the DVT and Trails B, but not for objectively measured long sleep duration. These results indicate a consistent association between self-reported, but not objectively measured, sleep duration and multiple aspects of cognition. No study to our knowledge has compared both relationships. This analysis helps to clarify the discrepant findings among studies examining TST and cognition. As with the current study, most previous results show an association with self-reported[8,9,12] but not objectively measured TST and cognition.[13,14,16] This may be due

Table 5—Sleep characteristics and DVT test completion time (sec)

Sleep Characteristic	Adjusted Means (95% CI) or β Coefficient (P-value)	R^2 for Model	Partial r^2 for the predictor	% of R^2 Explained by this predictor
Objective actigraphic parameters				
Sleep efficiency				
< 70%	531.5 (519.5, 543.8)	0.1505	0.0038	2.53
≥ 70% (ref)	530.6 (525.0, 536.4)	–	–	–
Continuous, per 1 SD decrease	1.18 (0.65)	0.1505	0.0056	3.72
Wake after sleep onset				
< 90 min (ref)	527.8 (521.7, 534.1)	–	–	–
≥ 90 min	537.4 (528.1, 546.9)	0.1513	0.0068	4.46
Continuous, per 30-min increase	**4.8 (< 0.01)**	0.1526	0.0152	9.98
Number of long wake episodes				
< 8 (ref)	530.2 (524.0, 536.5)	–	–	–
≥ 8	532.1 (523.1, 541.4)	0.1505	0.0034	2.26
Continuous, per 1 episode increase	0.59 (0.45)	0.1506	0.0069	4.56
Actigraphic total sleep time				
≤ 5 h	530.9 (515.9, 546.2)	0.1513	0.0012	0.81
> 5 to 7 h	527.6 (520.9, 534.4)	0.1513	0.0012	0.78
> 7 to 8 h (ref)	534.6 (524.3, 545.2)	–	–	–
> 8 h	543.2 (523.7, 563.3)	0.1513	0.0011	0.72
Continuous, per 1-h decrease	-1.98 (0.34)	0.1507	< 0.0001	0.01
Subjective sleep				
Self-reported total sleep time				
≤ 5 h	532.6 (517.5, 548.1)	0.1523	0.0015	0.98
> 5 to 7 h	529.3 (522.6, 536.0)	0.1523	0.0020	1.35
> 7 to 8 h (ref)	530.3 (520.5, 540.4)	–	–	–
> 8 h	**576.5 (552.7, 601.2)**	0.1523	0.0083	5.43
Continuous, per 1-h decrease	-4.61 (0.12)	0.1488	0.0002	0.11
Pittsburgh Sleep Quality Index				
≤ 5 (ref)	534.1 (527.1, 541.2)	–	–	–
> 5	530.2 (522.3, 538.1)	0.1483	0.0038	2.54
Continuous, per 1 SD increase	-2.54 (0.39)	0.1483	0.0073	4.93
Epworth Sleepiness Scale				
≤ 10 (ref)	531.7 (526.3, 537.2)	–	–	–
> 10	537.1 (522.5, 552.0)	0.1483	0.0017	1.14
Continuous, per 1 SD increase	0.49 (0.86)	0.1481	0.0015	0.98

Bold = P < 0.05. All results adjusted for age, race, clinic, BMI, instrumental activities of daily living, comorbidities, antidepressant use, benzodiazepine use, Geriatric Depression Scale score, education, alcohol use, smoking, physical activity, and self-reported health status.

to self-reported long sleepers perceiving TST to be much longer than it actually is due to awakenings throughout the night, or because they do spend more time in bed, but much of that time is spent awake. The average values for WASO showed a U-shaped pattern among categories of self-reported TST, which supports this idea. Also in support of this idea was the loss of association of self-reported long sleep duration with the Trails B and 3MS after further adjustment for WASO.

We found no association with self-reported poor sleep or excessive daytime sleepiness. This conflicts with other studies, which may be due to the differing populations studied.[10,11,20]

This study has several strengths. The study had a large population of community-dwelling older men who were not selected for inclusion based on sleep problems or cognitive impairment. There were a number of validated measures of sleep characteristics, including both subjective and objective measures. Adjustments for multiple potential confounding factors were made, suggesting these associations were not explained by other covariates including depression, comorbidities, medication use, education, or lifestyle.

This study also had several limitations. The findings may not be generalizable to populations groups other than community-dwelling older men. Causality cannot be established due to the cross-sectional study design. The association of cognition and sleep parameters may be bi-directional, so further research investigating direction of association on incident cognitive decline are needed. Adjustment for numerous covariates was performed, but there may be unmeasured confounders that may affect the results. An additional limitation is that our cognitive battery was somewhat limited and only included

measures of global cognition, vigilance, and executive function. The effect sizes are relatively small, and clinical meaningfulness is uncertain.

These findings suggest there was a modest association with objectively measured sleep fragmentation and self-reported long sleep duration and cognition among older community-dwelling men. Although self-reported long sleep duration was associated with cognitive deficits, this relationship may have been mediated by poorer sleep among the self-reported long sleepers. Further study needs to be done to examine if these associations hold for longitudinal cognitive decline.

ABBREVIATIONS

3MS, Modified Mini-Mental State examination
ANOVA, Analysis of variance
BMI, Body mass index
CHD, Coronary heart disease
COPD, Chronic obstructive pulmonary disease
DVT, Digit Vigilance Test
EDS, Excessive daytime sleepiness
ESS, Epworth Sleepiness Scale
GDS, Geriatric Depression Scale
IDIS, Iowa Drug Information Service
IADL, Instrumental activities of daily living
LWEP, Long wake episodes
MrOS, Osteoporotic Fractures in Men Study
PASE, Physical activity scale for the elderly
PSQI, Pittsburgh Sleep Quality Index
SE, Sleep efficiency
SOF, Study of Osteoporotic Fractures
TST, Total sleep time
WASO, Wake after sleep onset

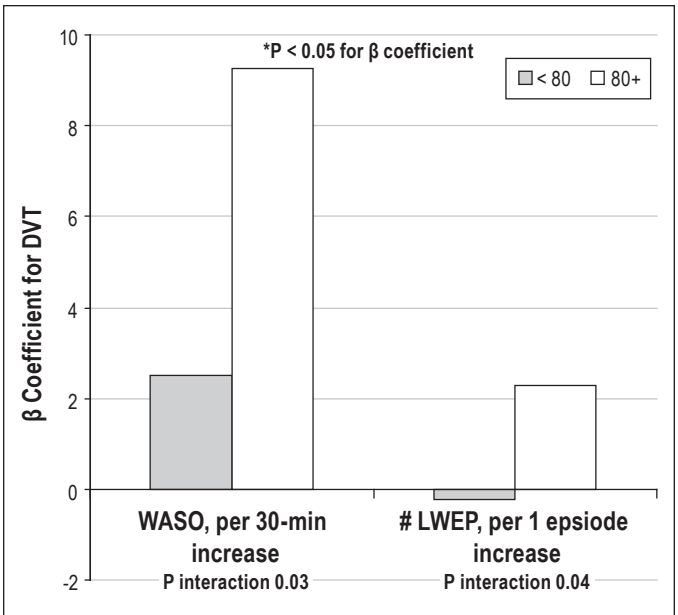

Figure 1—Interaction of Age with Sleep Fragmentation on DVT

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